October 12, 1953

Dear Dr. Felix:

One of your remarks in your letter of the 7th leads me think I have not adequately emphasized certain features of transduction, and especially how it differs from, for example, the determination of Vi phage type.

In a transduction experiment conducted within a given type, one may find that nearly every recipient bacterium that has been infected will engender lysogenic offspring. However, for any single trait, only about one per million of the lysogenic progeny will show any alteration, and alterations for different markers appear to be (generally) quite independent of one another. For this reason, transduction in Salmonella has been summarized as the adventitious carriage, in a small fraction of phage particles, of very small fragments of the hereditary material of the host bacterium to a new host. The preponderant majority of infected or lysogenized bacteria show no transductive changes. Alternatively, the transduction may occasionally be followed by a loss of the infecting phage, especially when this has been damaged by ultra-violet light, or when it is not well adapted to the new host. Nevertheless, the transduced factor remains stably fixed. We have thus concluded that the bacteriophage plays only an indirect role in Salmonella transduction: that of the initial fragmentation of the hereditary substance, and of carrying the fragments to a new cell. Otherwise, the process is quite analogous to the "transformations" of pneumococci and hemophilus, and I would consider these as another species of the genus transduction: in Salmonella, this is mediated by bacteriophage; in some other bacteria, by a bacteriologist. The situation is thus quite different from phage type determination and the transfer of toxicogenicity in Corynebacterium, in both of which, as I understand it, infection with phage is not merely a necessary but also a sufficient condition of the alteration.

I note your remark on the sequence of publications of Vi type determination, and will not conceal that I have had similar criticisms from others. I was quite aware of the priority of publication, and hope you would not regard my Ref. 3 as a subversion of it. In a limited space, I had to give those references that would most readily lead the reader to the current and previous literature on the subject, as the first paragraph of the review points out. The use of numbers rather than names would also support this plan, though not unequivocally. I would owe you an apology if I had given a false impression of priority (and, retrospectively, a direct reference to one of your general accounts of phage typing should have been given, though such references were available from #3).

I did not give Dr. Anderson many details on the transducing competence of k. This was shown (with the lysate as received!!) by the transduction of motility to non-motile variants S. typhi 0-901, S. typhimurium SW-1072, and S. paratyphi b (monophasic) SW-666, as well as the transfer of d to the last to give IV V XII d:-. I have not yet attempted any further trials with the O phages, but they are planned. As I hope I have now been able to clarify, O 901 can be made lysogenic for k, the restoration of motility being only an exceptional concomitant.

I am very pleased to learn that there was some substance to Creze's claims; some of his remarks were so obscure that I feared I would be wasting your time by referring him to you. In view of the established

spontaneous revertibility of H 901 to the Vi+ condition, it will be important to verify whether his technique "transfers" or "selects" the Vi+ character. My first guess would be for the latter.

To return again to your letter of January 1, I have recently essayed ~~transdu~~ transductions (e.g. of the flagellar i antigen) to Vi+ strains, such as Ty2. The results, though so far negative, are not yet conclusive owing to the interference of the Vi substance with optimal motility and possibly with the absorption of O phage. For the initial trials, another marker besides one depending on selective migration in semi-solid agar may be more appropriate.

I am pleased at your affirmative response to my request for reprints.

One last point that may interest you: as you may know, Dr. Aleck Bernstein who spent a year or so at the Standards Lab, before taking the Dipl. Bact., and a brief tour at Manchester] recently joined us. One of the first projects suggested was an attempt to confirm Sertic' claim (C. R. Soc. Biol. 123:951, 1936) of the differential agglutination by acriflavine of "non-specific", but not of "specific" flagellar phases. The claim has been clearly verified with several diphasic serotypes (typhimurium, stanley, london, zega and some others). Perhaps of some particular interest, the lw phase of S. wien was agglutinable (and not the b), while the enz_{18} phase of S. dar-es-salaam was agglutinable (and not the lw). All of which is in concordance with the genetic evidence of the division of ph1 and ph2 as distinct homology groups (i.e. sets of allels at two loci) and points to a far-reaching chemical difference between the two sets of factors. We are only just starting to think about the possibilities of chemical studies, having been favored with a brief visit from by C. Weibull (Uppsala).

We were rather surprised that Sertic' observation had not been scrutinized before (to our own knowledge!); do you know of any work on this question, published or not? Some experimental detail: the tests were started on slides, but the results are much clearer in tubes, set up much as for H-agglutination. Broth cultures, diluted perhaps up to 1:16 (or less), final concentration of acriflavine 1:2000, in saline 0.2% (probably no harm to use more), read after 4 hours at 37°. Boiled cells are inagglutinable; formalized cells of either phase are likely to agglutinate. The reaction resembles that of an H agglutination with antiserum.

One finds suspicions of other primary differences between the phases in the literature (e.g. differential motility) but I have not seen anything very tangible; are you acquainted with any work that might be pertinent?

Yours sincerely,

Joshua Lederberg